A STUDY ON CATEGORY II ANTI TUBERCULOSIS TREATMENT UNDER THE REVISED NATIONAL TUBERCULOSIS CONTROL PROGRAMME COVERED BY CHRISTIAN MEDICAL COLLEGE VELLORE

Dissertation submitted in partial fulfillment of the requirement of The Tamilnadu Dr. M.G.R. Medical University for Degree of M.D. Community Medicine examination (Branch XV) to be held in March 2007.

CERTIFICATE

This is to certify that **" A STUDY ON CATEGORY II ANTI-TUBERCULOSIS TREATMENT UNDER THE REVISED NATIONAL TUBERCULOSIS CONTROL PROGRAMME COVERED BY CHRISTIAN MEDICAL COLLEGE VELLORE"** is a bona fide work of Dr. Prashanth H.R in partial fulfilment of the requirements for the M.D. Community Medicine examination (Branch XV) of The Tamilnadu Dr. M.G.R. Medical University to be held in March 2007

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ACKNOWLEDGEMENTS

I would like to thank the following for their help and support during the preparation of this thesis:

- First and foremost, my guide, Dr K. R. John, but for whom I would have lost out on this rare opportunity to do this thesis on tuberculosis. I thank him for all the encouragement he gave me throughout the working out of this thesis and for making himself available whenever I needed him.
- To Dr. Jayaprakash Muliyil, Principal and Head of the department for his support, valuable ideas and guidance as always.
- To the RNTCP staff, and voluntary workers Mr. Sakthivel and Mr.Ravichandran who helped me in many ways.
- To all my consultants and colleagues, who were ready to help anytime.
- To Christian Medical College for offering me a generous research grant.
- To my parents who co operated with me always though bearing the difficulty of not seeing me for long times.
- To Dr. Venkat for his encouragement and valuable time.
- To all the staff of CHAD and CHTC for their help in various kinds.
- To D.D.G., TB the Central TB Division, D T O Vellore and his team for the success of the TB control programme.
- Finally for all my TB patients who shared their suffering to show the light for others in future.

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1. INTRODUCTION

Tuberculosis (TB) is a disease that has severely affected communities and nations since times immemorial. The disease has brought untold miseries to generations and even today, when newer modalities for diagnosis and treatment of TB have made the disease curable, people are suffering and dying from the disease.[1]

Tuberculosis remains the number one killer infectious disease affecting adults in developing countries. The 1990 World Health Organization (WHO) report on the Global Burden of Disease ranked TB as the seventh most morbidity-causing disease in the world, and expected it to continue in the same position up to 2020[2]

During 2004, it was estimated that about nine million new cases of TB occurred globally. India contributes a fifth of these cases, i.e., about 1.8 million, of which 0.8 million are new sputum-positive infectious cases. Nearly 400,000 estimated deaths occur annually due to tuberculosis. 75% of the people with tuberculosis are in the economically productive age group.[3]

The global community woke up to this disease when, in 1993, the WHO declared TB as a global emergency.[1]

The control of tuberculosis requires tremendous technical and managerial inputs. Tuberculosis control strategies have implemented a variety of operational elements through the history of its evolution. New approaches were introduced, as a result of a pressing need, a new discovery or a breakthrough in research. The current Directly Observed Treatment Short-course (DOTS) strategy is one such approach.

The DOTS strategy has shown encouraging results in areas where it has been implemented. It is based on a managerial approach to TB control with sound technical foundations. Its five core elements include sustained political commitment, short-course chemotherapy administered under proper case-management conditions, diagnosis primarily by sputum smear microscopy, regular drug supply and a sound monitoring system.[4]

The DOTS strategy for TB control recommended by the World Health Organization (WHO) is hailed as one of the most cost-effective of all health interventions to date.[5]

Under the DOTS Program patients are classified into 3 treatment categories—Categories I, II and III depending on the indication and previous history of treatment.

Category I is for New sputum smear-positive or Seriously ill sputum smear-negative or Seriously ill extra-pulmonary, treatment is with 2 Months of Isoniazid (H), Rifampicin(R), Pyrazinamide(Z) and Ethambutol(E) thrice a week, directly supervised followed by 4 months of isoniazid and rifampicin (**2H3R3Z3E3+4H3R3)**

Category II involves patients undergoing retreatment due to relapse, failure, default or others.

Cat II is treatment for a total duration of 8 months with 3 months of intensive phase comprising of **2 $H_3R_3Z_3E_3S_3$** and **1 $H_3R_3Z_3E_3$** followed by 5 months of continuation phase with **5 $H_3R_3E_3$**.(S= streptomycin)

Category III constitutes New sputum smear-negative, not seriously ill New extra-pulmonary, not seriously ill -**2H3R3Z3+4H3R3**

While many studies have been performed evaluating the efficacy of Category I treatment, not much is known about the effectiveness of anti-tubercular treatment for patients in Category II treatment.

2. BACKGROUND

Tuberculosis remains a major public health problem in India.
From January 2001 onwards, the externally funded Revised National Tuberculosis Control Programme (RNTCP) with its DOTS strategy officially began in Vellore district of Tamil Nadu.

Community health and development (CHAD) hospital run by the department of Community Medicine, Christian Medical College and Hospital (CMCH) Vellore, is functioning as a tuberculosis unit (TU) under the RNTCP. Vellore town patients are covered by the TB unit under Vellore District tuberculosis centre. There is an DOTS Clinic functioning in CMC hospital getting patients from all the departments of CMC. Annually around 600 patients will be started on Antitubercular Treatment (ATT) through the DOTS clinics and peripheral health systems. Cat II treatment constitutes about 10 – 15% of these cases.

One of the challenges in tuberculosis is treating patients who have failed initial attempts to cure their disease. These patients are moved into Category II in an attempt to provide further intervention.

The principal barrier to the elimination of tuberculosis is non-compliance with therapy by patients. The WHO has accordingly stressed the need for direct observation of therapy, which, as implied by the name, is the central feature of the widely advocated directly observed therapy short-course (DOTS) strategy[6]

While many studies have been performed evaluating the efficacy of Category I treatment, not much is known about the effectiveness of anti-tubercular treatment for patients in Category II treatment under the programme conditions.

The overall favourable re-treatment outcome in the Bangalore cohort was 39.8% as a result of a high proportion of 'defaults' (43.8%). However, favourable outcome among those completing the prescribed duration of treatment was75%, irrespective of pre-treatment drug susceptibility status. [8].

It is, however, now evident that non-compliance is not the fault of the patient but due to gross inadequacies in the provision of health care[7]

The argument against Cat II regimen for re-treatment cases by many physicians is the fear of adding a single drug to a failing regimen, causing emergence of further drug resistance, particularly MultiDrugResistence (MDR).

Does Category II treatment address the need to control refractory cases and non-adherent patients? Indeed, it is important to evaluate whether or not current attempts to control difficult tuberculosis cases with Category II treatment is effective.

Knowledge regarding risk factors for poor outcome will show areas of focus needed to increase effectiveness of Cat II treatment.

The present study is an attempt to address few of the above questions.

3. OBJECTIVES

1) To study the profile of tuberculosis patients on Category II treatment in a population covered by CHAD/ C M C H DOTS clinic under RNTCP .

2) To study outcome of treatment in the same patients after a time of followup as compared to the immediate outcome after treatment.

3) To study the risk factors associated with poor outcomes in the above group of patients

4. REVIEW OF LITERATURE

4.1 TUBERCULOSIS – AN OVERVIEW

TB is a **worldwide pandemic**; though the highest rates per capita are in Africa (29% of all TB cases), half of all new cases are in 6 Asian countries (Bangladesh, China, India, Indonesia, Pakistan, the Philippines).

2 billion people, equal to one-third of the world's total population, are infected with TB bacilli, the microbes that cause TB.[9]

TB is contagious and spreads through droplet infection; if not treated, each person with active TB infects on average 10 to 15 people every year.

According to WHO, TB infection is currently spreading at the rate of one person per second. It kills more young people and adults than any other infectious disease and is the world's biggest killer of women. In 1993, WHO declared TB to be "a global health emergency". Every year 8–10 million people catch the disease and 2 million die from it. Around 10% of people infected with TB actually develop the disease in their lifetimes, but this proportion is changing with HIV coinfections as HIV severely weakens the human immune system and makes people much more vulnerable.

In 2004, estimated per capita TB incidence was stable or falling in five out of six WHO regions, but growing at 0.6% per year globally. The exception is the African region, where TB incidence was still rising, in line with the spread of HIV. However, the number of cases notified from the African region is increasing more

slowly each year, probably because the HIV epidemics in African countries are also slowing. In eastern Europe (mostly countries of the former Soviet Union), incidence per capita increased during the 1990s, and peaked around 2001, but has since fallen.

In 2005, 46 African Health Ministers declared TB a regional **emergency in Africa**; the Regional Director for WHO's European Region also warned of a TB **emergency in Europe**.

The 2006 WHO report Global TB Control concluded that three (of six) WHO regions are likely to have met both the 2005 targets: the Region of the Americas and the South-East Asia and Western Pacific regions. Seven of the 22 high-burden countries are likely to have met the 2005 targets: Cambodia, China, India, Indonesia, Myanmar, the Philippines and Viet Nam within the 2005 timeframe, though final confirmation will come at the end of 2006.

India has the largest number of tuberculosis cases in the world.[4] Estimated prevalence of infection is 44% and of the disease is 505 per 1 00 000 population. Estimated incidence of pulmonary tuberculosis is about 187 per 1 00 000 and that of sputum smear for Acid Fast Bacilli positives is 84 per 1 00 000 in India.[10] Tuberculosis hinders the socioeconomic development of the country. 75% of people with tuberculosis are in the economically productive age group of 15–54 years. Besides the disease burden, TB also causes an enormous socio-economic burden on India. TRC, Chennai, undertook a study to estimate the socio-economic impact of tuberculosis in the country, from which it was

estimated that tuberculosis costs India more than $300 million annually in direct costs alone. Of this total, more than $100 million is incurred in the form of debt by patients and their families; and more than 100 million productive workdays are lost annually on account of tuberculosis

TRC has documented the economic impact (out-of-pocket expenses) of TB on patients and their families. Even though diagnosis and treatment are offered free of cost to patients, the average total cost was Rs 5,986 per patient amounting to about Rs 13,000 crores a year for the country[11]. More than 3,00,000 children may have left school permanently because of their parents' tuberculosis and 20 percent had to take up jobs in order to supplement the household income, especially if the father had TB., and more than 1,00,000 women were rejected by their families because of having tuberculosis,[12] thus TB, has the potential to impede the development of both individuals and society as a whole.

Review of studies investigating the economic impact of tuberculosis showed that, on an average, 3–4 months of work time are lost if an adult has tuberculosis, resulting in the loss of 20–30% of annual household income, and an average of 15 years of income is lost if the patient dies from the disease[3]

By and large, prevalence figures are not quoted in most Indian references due mainly to the lack of consensus on data about the duration of the disease in the absence of any interventions. A recent study by the Tuberculosis Research Centre (TRC), Chennai, gives the average duration of the disease as three-and-a-half years.[13] However, the sample taken may not be sufficient to extrapolate to the whole of India.

4.2 THE HISTORY OF TUBERCULOSIS CONTROL

4.2.1 EVOLUTION OF WHO TUBERCULOSIS CONTROL POLICIES

The policies of the WHO went through various stages as experience was gained from therapeutic trials to field operations in different countries. [14,15]

Vertical programs that were successful in developed countries between 1948 and 1963 were found unsuitable for poorer nations due to lack of resources.[16] Integration of tuberculosis control services into the general health services was then tried with equally unimpressive results.[17,18]

Managerial integration and health sector reform came in the 1980s, which further pushed for decentralisation. This, however, led to the further weakening of the TB control structure as the TB experts were side-lined and policies were dumped on an unprepared peripheral health setup.[19]

This dismal state of affairs in TB control, fuelled by the HIV epidemic and socio-economic and political turmoil, led to its increased incidence in both developed and developing nations.[20,21] With this alarming state of affairs, the WHO defined a new control strategy in 1991.[22] WHO embarked on the promotion of an approach that was successfully implemented by K. Styblo of the IUATLD in some

of the poorest African countries, like Tanzania and Malawi. It set global targets for tuberculosis control of 85% cure and 70% case detection. In 1995, this framework was packaged and promoted aggressively under the brand name Directly Observed Treatment Short-course, or "**DOTS**".[23]

A variety of interventions have been evolved over the years to increase the compliance of patients to anti-tuberculosis treatment. The major inputs have been:

- Domiciliary treatment - 1956
- Supervised swallowing of drugs, also know as Directly Observed Treatment (DOT) - 1958
- Intermittent dosing of drugs – 1961 to 1977
- Short Course Chemotherapy (SCC) – 1972 to 1976
- Direct Observation of Treatment Short course (DOTS) strategy – 1991[24]

4.2.2 INDIA - NATIONAL TUBERCULOSIS PROGRAMME 1962

National Tuberculosis Institute (NTI) was established in 1959 to evolve through research a practicable TB programme that could be applied in all parts of the country. The National tuberculosis programme (NTP) which was started in 1962 created an extensive infrastructure for tuberculosis control and has succeeded in placing more than 13 lakh patients on treatment on a yearly basis. Based on the findings of the operational studies conducted, a draft recommendation for the District Tuberculosis Programme (DTP) was prepared in 1961, keeping in mind

an average Indian district, its population and health facilities available. Anantapur district in Andra Pradesh was chosen to establish the first model district TB centre (DTC).

The National Tuberculosis Programme (NTP) policy as enunciated in the introduction manual of DTP comprised:

- Domiciliary treatment
- Use of a standard drug regimen of 12-18 months duration
- Treatment free of cost
- Priority to newly diagnosed patients, over previously treated patients
- Treatment organization fully decentralized
- Efficient defaulter system/mostly self-administered regimen
- Timely follow up
- Chemoprophylaxis not recommended as it is impractical on mass basis.

NTP was a decentralized programme with District TB Centres (DTC) established for implementation of the programme at the district level. Below the level of district, it is integrated into the general health services provision through the network of Primary Health Centres and first and second level referral health institutes. The major objectives of the NTP were to diagnose as large a number of cases as possible and provide efficient treatment placing priority on smear

positive patients; and to implement those activities in an integral part of general health services.

Under the NTP, the TB symptomatics have been by and large referred to the District Tuberculosis Centers (DTC) located at District head quarters for diagnosis. The patients who were diagnosed TB were referred back to the nearest Primary Health Centre from where the patients collected their drugs once a month for self administration at home. The patients returned to the DTC for the follow up check ups or for the treatment of side effects.

In 1992 the Indian government undertook a joint review of the tuberculosis situation with the help of the WHO and the Swedish International Development Agency (SIDA). Based on these recommendations, the government of India came up with the Revised National Tuberculosis Control Program (RNTCP) in 1993 which is the Indian version of the 'DOTS Strategy'.[13]

4.2.3 THE REVISED NATIONAL TUBERCULOSIS CONTROL PROGRAMME (RNTCP)

In the light of the recommendations and concerns expressed by the Central Health Council, steps were taken since 1993 to implement the Revised National Tuberculosis Control Programme (RNTCP) in selected areas with World Bank assistance[25]

The RNTCP strengthens the existing NTP infrastructure by creating a sub-district-level supervisory team (known as the TB Unit), consisting of a treatment supervisor (Senior Treatment Supervisor, STS) and a laboratory supervisor (Senior TB Laboratory Supervisor, STLS). These are new posts. In addition, a medical officer from the general health system serves as Medical Officer—TB Control at sub-district level who is specifically allocated tuberculosis control duties in addition to his/her other duties.

These 3 individuals constitute the management unit, which is responsible for overseeing operations in approximately a 5 lakh population including, on average, 5 designated microscopy centres. At each microscopy centre, a state-of-the art binocular microscope, good quality reagents and new recording and reporting proformae are available. More importantly, intensive modular training, supervision, and cross-checking of the work of the laboratory technician ensure that reliable results are obtained.[25]

Starting in October 1993, the RNTCP was implemented in a population of 2.35 million in 5 sites in different states (Delhi, Kerala, West Bengal, Maharashtra, and Gujarat). The programme was expanded to a population of 13.85 million in 1995 and 20 million in 1996. RNTCP thereafter expanded rapidly to cover 30% of the population by 2000, 50% of the population by end 2002 and 87% of the population (approximately 947 million people) as of end 2004. This is spread

across 547 districts of the 31 states and Union Territories (UTs) in India, with 26 states and UTs being fully covered.

Population coverage by RNTCP in March 2005 has gone up to 1001 million (1 billion) 90% coverage. It was targeted to cover the entire country by the end of 2005[26].

BASIC PRINCIPLES OF THE RNTCP – DOTS STRATEGY

The basic principles of the RNTCP are[27]

1. Political commitment to ensure adequate funds, staff, and other key inputs.

2. Diagnosis primarily by microscopic examination of the sputum of patients presenting to health facilities.

3. Regular and uninterrupted supply of anti-TB medications including the use of a patient-wise box which contains the entire course of treatment for an individual patient so that no patient should ever stop treatment for lack of medicines.

4. Direct observation of every dose of treatment in the intensive phase and at least the first dose in the continuation phase of treatment,

5. Systematic monitoring, supervision and cohort analysis.

One Senior Treatment Supervisor (STS) for organization of uninterrupted treatment and one Senior Tuberculosis Laboratory Supervisor (STLS) for ensuring quality laboratory service for every 5 lakh population. Additional staff are provided for difficult hilly, tribal, and some urban areas.

If 3 AFB smears are negative and there is no response to 1-2 weeks of antibiotics, X-ray is taken, and, if consistent with TB, the patient is treated for smear-negative TB. If only one of three specimens is positive, an x-ray is taken and the patient is evaluated. All treatment is given thrice weekly on alternate days. During the intensive phase, every dose is directly observed; medications for the continuation phase are packaged into a weekly blister pack, at least the first dose of which is directly observed.

Policy direction, supervision, drugs and microscopes are provided by the Central Government. Districts receive funds directly from the Central Government out of the World Bank or Danida assistance[22]. Multi-purpose workers are responsible for treatment observation. In areas where they are not available, treatment observation is done by community volunteers including Anganwadi workers, traditional dais, and community and religious leaders. Observation by a family member is not acceptable in the programme[26]. For the success of the Tuberculosis treatment the DOTS providers must be organized in patient's convenience rather than the convenience of the treatment service providers.

The goal of RNTCP is to cure at least 85% of new smear-positive cases of tuberculosis and to detect at least 70% of such patients, after the desired cure rate has been achieved. Clearly, both good outcomes and high case detection rates are essential. Curing the patients reliably results in a "recruitment effect" – wherever effective services are offered, case detection rates steadily increase.

Cured patients act as one of the best motivators promoting case detection and patient adherence to treatment.

Perhaps the greatest strength of the RNTCP is the new recording and reporting system. This system ensures accountability for each and every patient started on treatment. RNTCP shifts the responsibility for cure from the patient to the health system

The “Stop TB” Department in the World Health Organization has developed a strategy called “Public–Private Mix DOTS” (PPM-DOTS). The strategy consists of DOTS implementation in the private sector according to WHO guidelines, provision of free drugs and some financial support by the government, strengthened collaboration between public and private providers through improved referral and information systems, contracts between the public and private sectors, and continuous dialogue.PPM-DOTS can be an effective, affordable and cost-effective approach to improving TB control in India[28]

The costs of the programme have been consistently low, with lower-than-expected unit cost of drugs and microscopes. A full course of anti-TB drugs costs less than US$ 7 per patient. The total programme expenditure has been approximately US$ 0.05 per person covered per year.[29]

4.3 PROBLEMS WITH TB CONTROL -- Continuing challenges

Despite having a definitive cure and its pathogenesis well understood, tuberculosis remains a major unsolved health problem of worldwide dimensions. Why has this happened? Anti-tuberculosis treatments (ATT) are comparatively long, and even with present day short course chemotherapy, six months of regular drug intake is mandatory. Almost without exception, experts acknowledge the role of patient compliance to treatment as one of the major contributing factors to this dilemma.[30] It may be, as Addington put it, "The most serious remaining problem in the control of tuberculosis…is non adherence".[31]

4.3.1 Multidrug-resistant TB (MDR-TB) is a form of TB that does not respond to the standard drug treatment. MDR-TB is present in virtually all 109 countries recently surveyed by WHO and partners.

450 000 new MDR-TB cases are estimated to occur every year. The highest rates of MDR-TB are in countries of the former Soviet Union and China.

Projects managing MDR-TB can apply through the **Green Light Committee** for access to quality assured MDR-TB drugs at reduced prices – in some cases by more than 90%.The Committee is operated by WHO and the StopTB partnership.

NTI, Bangalore conducted drug resistance surveillance (DRS) in the four districts of Mysore (2001), Hoogly (2003), Mayurbhanj (2003) and also in Bangalore city (1999) where MDR-TB levels amongst patients with no history of previous treatment were observed to be 1.2 percent, 3.0 percent, 0.7 percent, and 2.2 percent, respectively (NTI 2003)10,11,12. The above data can be considered to

represent a fairly accurate picture of true primary resistance. the multi-drug resistance in previously treated cases was found to be 12.8 percent and ranged from 8.4 to 17.2 percent.[32]

4.3.2 TB and HIV/AIDS a lethal combination, each speeding the other's progress. Because HIV weakens the immune system, someone who is HIV/TB co-infected is many times more likely to become sick with TB than someone infected with TB who is HIV-negative. TB is a leading cause of death among people who are HIV-positive, accounting for approximately 13% of AIDS-related deaths worldwide. In Africa, HIV is the single most important factor determining the increased incidence of TB over the past 10 years. In 2004, out of an estimated 8.9 million new TB cases worldwide, 3.9 million were diagnosed by laboratory testing and 741,000 also were HIV-positive. An estimated 1.7 million people died of TB in 2004, 15% of whom were coinfected with HIV.TB accounts for up to a third of AIDS deaths worldwide.

Improved collaboration between TB and HIV/AIDS programmes will lead to more effective control of TB among HIV-infected people and to significant public health gains.HIV-positive people can easily be screened for TB; if they are infected they can be given prophylactic treatment to prevent development of the disease or curative drugs if they already have the disease. TB patients can be offered an HIV test; indeed, research shows that TB patients are more likely to accept HIV testing than the general population. This means TB programmes can make a major contribution to identifying eligible candidates for ARV treatment.

4.3.3 RELAPSE IN TUBERCULOSIS

Relapse is defined as “a patient previously treated for tuberculosis who has been declared cured or treatment completed, and is diagnosed with bacteriologically positive (smear or culture) tuberculosis”.[33] The goal of tuberculosis treatment is to ensure relapse-free cure while preventing the emergence of drug resistance. Use of a four-drug regimen in DOTS strategy reduces the risk both of drug resistance developing and of failures and relapses. If a patient defaults on treatment after the initial intensive phase, relapse is less likely[34].

In a longitudinal survey and analytical studies, it was found that relapse still accounted for about 15–20% of the annual incidence of newly registered infectious cases. Controlled clinical trials in which patients were followed up regularly for 2 years or more have shown that the frequency of relapse is around 3–7% with standardized short-course chemotherapy. The relapse rates in randomized-controlled trials of SCC done in India showed a relapse rate of 5.8% to 15.3% (Appendix IV). More than 80% of relapses occur with organisms susceptible to the tuberculosis drugs used earlier.[35]

The individual risk of relapse among persons with a history of bacteriologically confirmed tuberculosis varied substantially and was determined mainly by the factors whether or not the regimen given was adequate and regularly taken; and the time that had elapsed since smear / culture conversion to negative was achieved. Approximately 80% of the relapses occur within 6 months of stopping

treatment.[33]The WHO recommended DOT has the positive influence on bringing down the relapse.

4.3.4 Treatment failure is defined as continued or recurrently positive smears during the course of antituberculosis therapy. After 3 months of multidrug therapy for pulmonary tuberculosis caused by drug-susceptible organisms, 90--95% of patients will have negative smears and show clinical improvement. Thus, patients with positive smears after 3 months of what should be effective treatment must be evaluated carefully to identify the cause of the delayed conversion. Patients whose sputum smears remain positive after 4 months of treatment should be deemed treatment failures.

The main reasons for failure are premature cessation of treatment (default) and irregularity in taking drugs, prescription of inadequate regimens, drug resistance, delay in starting treatment, drug toxicity, malabsorption of drugs, laboratory error, and extreme biological variation in response. If treatment failure occurs, early consultation with a specialty center is strongly advised. If failure is likely due to drug resistance and the patient is not seriously ill, an empirical retreatment regimen could be started or administration of an altered regimen could be deferred until results of drug susceptibility testing from a recent isolate are available. If the patient is seriously ill or sputum AFB smears are positive, an empirical regimen should be started immediately and continued until susceptibility tests are available. For patients who have treatment failure, *M.*

tuberculosis isolates should be sent promptly to a reference laboratory for drug susceptibility testing to both first- and second-line agents.

4.3.5 Defaulting Treatment and Side-effects: Obstacles to Managing Patients?

The failure to take medications as prescribed is a universal and perplexing phenomenon that must always be taken into consideration in any efforts to treat patients or control disease in a community. Adherence to treatment is one of the biggest challenges facing both TB patients and the TBcontrol programmes. "DOTS treatment is intensive and requires on-going commitment and responsibility of each patient". It is commonly accepted by many health care workers that poor adherence to treatment is mainly a problem arising from misconceptions of the patient about the disease and its treatment. Health education is therefore usually seen as the most powerful tool to overcome defaulting in treatment. However, human behaviour is complex and there is no single psychosocial construct for health behaviour that is reliable and accurate in predicting treatment adherence, including TB.

The expense of treatment, in terms of both time and money, is a further deterrent to patient compliance. Complicated regimens are associated with even higher default rates. An operational research project conducted between 1996 and 1998 to assess the needs and perspectives of patients and providers in two chest clinics in Delhi, Moti Nagar and Nehru Nagar, during the introduction of the new strategy concludes that the reasons for default stem from a poor correlation between patient and programme needs and priorities, and from particular

characteristics of the disease and its treatment. Patient needs that were not met by the health system included convenient clinic timings, arrangements for the provision for treatment in the event of a family emergency and provision for complicated cases like alcoholics. The problems facing the provider were poor interpersonal communication with the health staff, lack of attention and support at the clinic, difficulty for patients to re-enter the system if they missed treatment and, in certain areas, long distances to the clinic. Problems related to diseases were inability of the staff to deal with drug side-effects, and patients' conception of equating well-being with cure. Simple, practical measures could improve the provision of tuberculosis (TB) treatment: more flexible hours, allowances for poor patients to reach the clinics and training health care staff for respectful communication and monitoring drug side-effects. The findings indicate a need to rethink the label of 'defaulter' often given to the patients. The important areas for future operational research is also highlighted. [36]

Thus, the key to treatment success is to be found in the organization of the delivery and adequate administration of treatment. Even the best available regimen will have a low success rate if treatment services are not focused on facilitating patient access to care and ensuring regular drug intake.

4.3.6 Extrapulmonary Tuberculosis

Tuberculosis can involve virtually any organ or tissue in the body. Nonpulmonary sites tend to be more common among children and persons with impaired immunity. EPTB cases form a significant proportion (8-14 percent) of the RNTCP's new case load.

RNTCP classification of extrapulmonary TB:

Seriously ill TB meningitis, Disseminated TB, TB pericarditis, TB peritonitis & intestinal TB, Bilateral or extensive pleurisy,Spinal TB with neurological Complications, Genito-urinary tract

Not seriously ill_ Lymph node TB Pleural effusion (unilateral) , Bone (excluding spine) , Peripheral joint(s)

To establish the diagnosis of extrapulmonary tuberculosis, appropriate specimens including pleural fluid; pericardial or peritoneal fluid; pleural, pericardial, and peritoneal biopsy specimens; lymph node tissue; and bone marrow, bone, blood, urine, brain, or cerebrospinal fluid should be obtained for AFB staining, mycobacterial culture, and drug susceptibility testing (*1*). Tissue specimens should also be examined microscopically, after routine and AFB staining, but the absence of AFB and of granulomas or even failure to culture *M. tuberculosis* does not exclude the diagnosis of tuberculosis. Bacteriological evaluation of the response to treatment in extrapulmonary tuberculosis is often limited by the difficulty in obtaining follow-up specimens. Thus, response often must be judged on the basis of clinical and radiographic findings. In developing

countries, the lack of diagnostic resources adds to the problems.This often leads to empirical treatment based on clinical grounds without pathological and/or bacteriological confirmation, leading to over-diagnosis and unnecessary treatment. This was shown in a study at TRC, Chennai, where only 34 percent of 373 biopsies done on clinically diagnosed cases of LNTB, had histopathological confirmation[37].

FEW STUDIES ON CAT II ATT:

i) RE-TREATMENT OUTCOME OF SMEAR POSITIVE TUBERCULOSIS CASES UNDER DOTS IN BANGALORE CITY

1) A cohort of 226 smear and culture positive re-treatment cases, initiated on Cat II regimen under DOTS, was followed up prospectively from April 1999 to September 2001, in Bangalore to study the treatment outcome along with the drug susceptibility status. The overall favourable re-treatment outcome in the cohort was only 39.8% as a result of a high proportion of 'defaults' (43.8%). However, favourable outcome among those completing the prescribed duration of treatment was 75%, MDR –TB among the cohort was 12.8%.[8]

2) As presented by Dr. Fraser Wares – WHO India 'RNTCP CAT II regimen in retreatment cases' at the research dissemination workshop Chennai, Jan 2005, of the cases from 1997 – 2003 India with a sample size of 2,57,442, a cure rate of 67.2% and default rate of 15.2% were noted. [38]

3) In yet another study carried to evaluate outcome of DOTS treatment by S.L.Chadha and R-P.Bhagi 1999-2000 at municipal corporation of Delhi, cure rate of 73.3% and default rate of 16% with 104 cat II treatment patients was published[39]

4)Vishal Verma, et al Dept. of Tuberculosis & Respiratory Diseases, Amritsar, India undertook a study to determine the treatment outcome of DOTS as prescribed under RNTCP in 2003. Side effects and radiological improvement was also noted. 150 cases of tuberculosis were followed. Cure rate was 91% & 71.40% for category I & II. Treatment completion rate was 100% for category III. Overall default rate was 5.33%. Failure rate was 0.67%.[40]

THE FUTURE IN TUBERCULOSIS CONTROL ---

The Stop TB Strategy was launched by W H O in January 2006.[40,41]

Vision - A WORLD FREE OF TB

Goal - To dramatically reduce the global burden of TB by 2015 in line with the Millennium Development Goals and the Stop TB Partnership targets

Objectives

Achieve universal access to high-quality diagnosis and patient-centred treatment

Reduce the human suffering and socioeconomic burden associated with TB

Protect poor and vulnerable populations from TB, TB/HIV and MDR- TB

Support development of new tools and enable their timely and effective use

Targets

MDG 6, Target 8: ...halted by 2015 and begun to reverse the incidence.....

Targets linked to the MDGs and endorsed by the Stop TB Partnership:

– by 2005: detect at least 70% of new sputum smear-positive TB cases and cure

at least 85% of these cases

– by 2015: reduce prevalence of and death due to TB by 50% relative to 1990

– by 2050: eliminate TB as a public health problem (<1 case per million population)

Save an additional 14 million lives

Treat 50 million people for TB[43]

Put 3 million TB patients coinfected with HIV onto antiretrovirals

Treat 800 000 people for MDR-TB

Produce the first new anti-TB drug in 40 years by 2010

Develop a new vaccine by 2015

COMPONENTS OF THE STOP TB STRATEGY

1. Pursue high-quality DOTS expansion and enhancement

a. Political commitment with increased and sustained financing
b. Case detection through quality-assured bacteriology
c. Standardized treatment with supervision and patient support
d. An effective drug supply and management system
e. Monitoring and evaluation system, and impact measurement

2. Address TB/HIV, MDR-TB and other challenges

- Implement collaborative TB/HIV activities
- Prevent and control multidrug-resistant TB

- Address prisoners, refugees and other high-risk groups and special situations

3. Contribute to health system strengthening

- Actively participate in efforts to improve system-wide policy, human resources, financing, management, service delivery, and information systems
- Share innovations that strengthen systems, including the Practical Approach to Lung Health (PAL)
- Adapt innovations from other fields

4. Engage all care providers

- Public-Public, and Public-Private Mix (PPM) approaches
- International Standards for Tuberculosis Care (ISTC)

5. Empower people with TB, and communities

- Advocacy, communication and social mobilization
- Community participation in TB care
- Patients' Charter for Tuberculosis Care

6. Enable and promote research

- Programme-based operational research
- Research to develop new diagnostics, drugs and vaccines

- Provide rapid and inexpensive diagnostic tests at the point of care

Full funding of the **Global Plan to Stop TB 2006– 2015** over the next 10 years will cost US$ 56 billion, and represents a three-fold increase in investment. The estimated funding gap is US$ 31 billion must be bridged. This is equivalent to just US$ 2 a year from every person in the industrialized world.

WHO Director-General Dr LEE Jong-wook said: “There is clear evidence that investment in TB control works. Even in low-income countries with enormous financial constraints, programmes are operating effectively and producing results. This same commitment needs to be replicated in African countries and other areas where funding and priority for TB control remains fragile.[44]

5. METHODOLOGY

STUDY DESIGN: Non-concurrent cohort study. Patients followed up retrospectively from standard RNTCP treatment cards, belonging to Category II Antitubercular treatment in a population covered by C M C H DOTS clinic.

Patients and Methods

All the Patients started on CAT II ATT registered under DOTS in CHAD/CMC from January 2001 to December 2004 were considered for the study. Information regarding the indication of treatment, the Sputum conversion rates and the outcome of treatment at the end of one year such as Cure, default, death, completion rate, and failure were analyzed in detail.

All Patients from geographically accessible areas (including Kaniyambadi block and Ussoor, Poigai, Pallikonda PHC areas) were followed up in their homes to know the present condition, interviewed using a pretested questionnaire and 2 sputum samples were collected from all symptomatic patients.

The relapse rates were estimated based on followup sputum AFBs and cultures.

Risk factors associated with poor outcomes viz death, default, relapse and failure analyzed by patient/ patient relative's interviews.

Inclusion Criteria: Patients started on CAT II ATT between JAN 2001 – DEC 2004 under RNTCP DOTS regime in CHAD/CMC DOTS clinic.

Exclusion Criteria: Children<15 years (paediatric DOTS).

Outcome Measures:

Default rate

Treatment completion rate

Cure rate

Treatment failure rate

Relapse rate over time of follow up

Sputum AFB and sputum Culture status of the patients who are symptomatic during the follow up.

Risk factors leading to poor outcomes – default, failure and relapse.

.

Definition of terms: Type of Case[6]

Relapse—A patient declared cured of Tuberculosis by a physician but who reports back to the health service and is found to be bacteriologically positive.

Failure—Smear positive patient who remains smear positive at 5 months or more after starting treatment. It also includes a patient who was initially smear negative but becomes smear positive during treatment.

Treatment after Default—A patient who received antituberculosis treatment for one month or more and returns to treatment after having defaulted, i.e. not taken anti-tb drugs consecutively for 2 months or more.

Other - Patients who do not fit into the above mentioned categories. Reasons for putting a patient in this category must be specified.

Definitions: treatment outcomes[6]

Cured -Initially smear+ve patient who has completed treatment and had negative sputum smears, on at least two occasions, one of which was at completion of treatment.

Treatment completed -Sputum smear+ve case who has completed treatment, with negative smears at the end of the initial phase but none at the end of treatment Or: Sputum smear-ve patient Or: Extra-pulmonary patient who has received a full course of treatment and has not become smear+ve during or at the end of treatment.

Success - The sum total of patients 'Cured' and 'Completed' treatment.

Died - Patient who died during treatment, regardless of cause

Failure - Any TB patient who is smear+ve at ≥5 months after starting treatment. Failure also includes a patient who was treated with Category III regimen but who becomes smear+ve during treatment.

Defaulted - A patient who, at any time after registration, has not taken anti-TB drugs for 2 months or more consecutively.

Relapse - A patient declared cured of Tuberculosis and bacteriologicaly negative at completion of treatment but who reports back to the health service and is found to be bacteriologically positive on followup.

Sample size:

4pq/d2

p= prevalence (assuming 50% success rate of Cat II on followup)

q= 1-p

d= 20% relative precision

Sample Size= $4(.5*.5) / (0.1)^2 = 100$

Assuming 10% loss to follow-up, sample size of **110**

Data entry and statistical analysis was done using Epi Info version 3.2.2 from CDC, Atlanta and SPSS data analysis package version 12.0. Comparison of treatment success, death, relapse rates and risk factors for poor outcomes was done using appropriate statistical tests.

6. RESULTS

ANALYSIS OF ALL PATIENTS WHO HAD CAT II ATT FROM 2001 TO 2004 FROM CHAD/CMCH DOTS CLINICS.

6.1 BASELINE CHARACTERISTICS

Table 6.1.1 YEAR WISE BREAK UP OFALL PATIENTS TREATED UNDER RNTCP FROM CMCH FROM 2001 TO 2004

YEAR	TOTAL PATIENTS	CAT II
2001	448	82 (18.3%)
2002	645	97(15.3%)
2003	623	65(10.4%)
2004	629	65(10.3%)
TOTAL	2345	309(13.2%)

.

Table 6.1.2 INDICATION FOR CAT II TREATMENT

	NUMBERS	PERCENTAGE
RELAPSE	197	63.8
DEFAULT	61	19.7
FAILURE	29	9.4
OTHERS	21	6.8
TRANSFER IN	1	0.3
TOTAL	309	

Table 6.1.3.1 AGE DISTRIBUTION OF PATIENTS ON CAT II ATT

	Frequency	Percent	Cumulative Percent
<20	15	4.9	4.9
21-30	73	23.9	28.8
31-40	75	24.3	53.1
41-50	72	23.3	76.4
51-60	52	16.8	93.2
61-70	18	5.8	99.0
>70	3	1	100.0
Total	309	100.0	

GRAPH 6.1. AGE DISTRIBUTION OF ALL CASES.

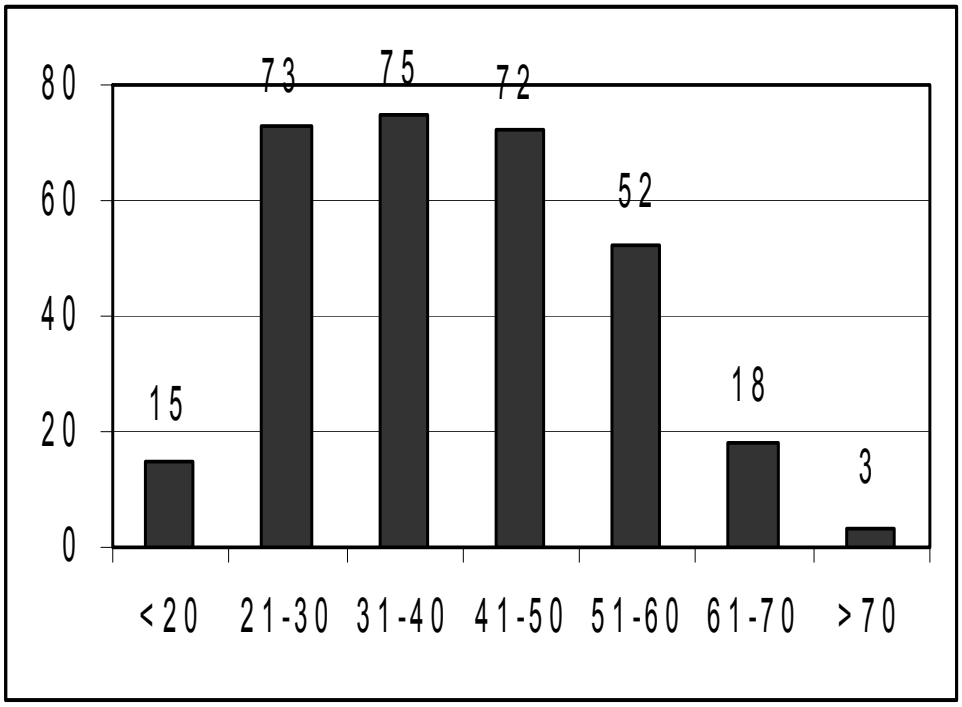


TABLE6.1.3.2 AGE AND SEX DISTRIBUTION OF ALL CAT II CASES

AGE GROUPS	MALES	FEMALES
<20	**6** (2.4%)	**9**(15.8%)
21-30	**50**(19.8%)	**23**(40.3%)
31-40	**64**(25.4%)	**12**(21.1%)
41-50	**64**(25.4%)	**8**(14%)
51-60	**48**(19%)	**4**(7%)
61-70	**17**(6.7%)	**1**(1.8%)
>70	**3**(1.2%)	0
Total	**252**	**57**

GRAPH 6.1.3.2 AGE AND SEX DISTRIBUTION OF ALL CAT II CASES

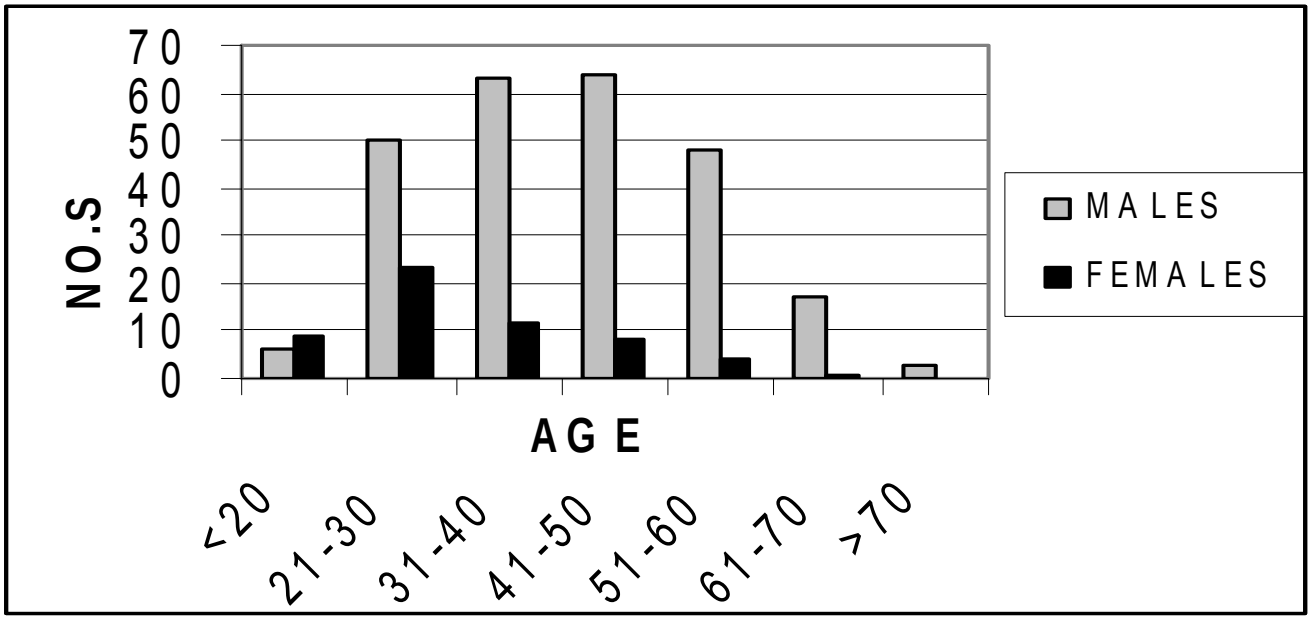


Table 6.1.4 TYPE OF CASE

CASES	Frequency	Percent
EXTRA PULMONARY	13	4.2
PULMONARY	296	95.8
Total	309	100.0

Table 6.1.5 SPUTUM STATUS AT INITIATION OF TREATMENT.

	NUMBERS	PERCENTAGE
1+	131	42.4
2+	71	23.0
3+	81	26.2
NEG	9	2.9
NOT AVAILABLE	11	3.5
SCANTY	5	1.5
NUMEROUS	1	0.3
TOTAL	309	

Table 6.1.6 OUTCOME OF ALL PATIENTS AT THE END OF INITIAL TREATMENT

(N=309)	NUMBERS	PERCENTAGE
CURED/COMPLETED	197	63.8
DEFAULT	46	14.9
EXPIRED	41	13.3
FAILURE	19	6.1
TRANSFERRED OUT	06	1.9

Table 6.1.7 INDICATION OF TREATMENT VS OUTCOME OF TREATMENT

		OUTCOME OF TREATMENT					
INDICATION OF TREATMENT		SUCCESS	DEFAULT	EXPIRED	FAILURE	TRANSFER	TOTAL
	DEFAULT	35(57.3%)	14(23%)	9(14.7%)	2(3.3%)	1(1.7%)	61
	FAILURE	17(58.6%)	2(6.9%)	3(10.3%)	7(24.2%)	0	29
	OTHERS	18(85.7%)	1(4.8%)	2(9.5%)	0	0	21
	RELAPSE	127(64.5%)	29(14.7%)	27(13.7%)	10(5.1%)	4(2%)	197
	TRANSFER IN	0	0	0	0	1	1
	TOTAL	197	46	41	19	6	309

FOLLOW UP STUDY RESULTS- 6.2

TABLE 6.2.1 NUMBER OF PATIENTS FOLLOWED-UP

YEAR	TOTAL CAT II PATIENTS	PATIENTS FOLLOWED UP
2001	82	18
2002	97	36
2003	65	32
2004	65	24
TOTAL	309	110

TABLE 6.2.2 INDICATION FOR TREATMENT IN PATIENTS FOLLOWED-UP

	NUMBER OF PATIENTS	PERCENTAGE
RELAPSE	71	64.5
DEFAULT	21	19.1
FAILURE	8	7.3
OTHERS	10	9.1
TOTAL	110	100

TABLE 6.2.3 INITIAL OUTCOME OF TREATMENT IN PATIENTS FOLLOWED-UP

	NUMBER OF PATIENTS	PERCENTAGE
TREATMENT SUCCESS	80	72.7
DEFAULT	25	22.7
FAILURE	5	4.6
TOTAL	110	100

TABLE 6.2.4LITERACY STATUS OF PATIENTS FOLLOWED-UP

	NUMBER OF PATIENTS	PERCENTAGE
ILLITERATE	33	30
READ AND WRITE	68	61.8
READ ONLY	9	8.2
TOTAL	110	100

TABLE 6.2.5 CAUSES FOR INTERUPTION OF TREATMENT AS TOLD BY PATIENTS

SIDE EFFECTS	12
SEVERELY ILL	3
OUT OF STATION	27
FELT BETTER	3
LACK OF AWARENESS	2
NOT CONVINCED OF TB DIAGNOSIS	2
NO FAMILY SUPPORT	1
OTHER CAUSES	5

TABLE 6.2.6 ORIGIN OF CAT II (H/O CAT I TREATMENT FROM)

	Frequency	Percent	Valid Percent
RNTCP	**57**	**51.8**	**71.3**
PRIVATE	**23**	**20.9**	**28.8**
Total	**80**	**72.7**	**100.0**
NOT TRACEABLE	**30**	**27.3**	
Total	**110**	**100.0**	

NOT TRACEABLE ARE MORE FROM THE DEATH GROUP

TABLE 6.2.7 FOLLOW-UP SPUTUM RESULTS

	NUMBER OF PATIENTS
NEGATIVE	62
1+	1
3+	1
NOT AVAILABLE*	46
TOTAL	110

*SPUTUM NOT AVAILABLE INCLUDES PATIENTS WHO ARE DEAD AND ALSO PATIENTS WHO WERE LOST TO FOLLOWUP.

TABLE 6.2.8 CURRENT STATUS OF PATIENTS FOLLOWED-UP

	NUMBER OF PATIENTS	PERCENTAGE
SUCCESS	64	58.1
DEATH	35	31.8
RELAPSE	2	1.8
LOST TO FOLLOW-UP	5	4.5
RETREATED	4	3.6
TOTAL	110	100

TABLE 6.2.9 INITIAL OUTCOME VS CURRENT STATUS ON FOLLOW-UP

		CURRENT STATUS					
		SUCCE-SS	**DIED**	**LOST**	**RELA-PSE**	**RETREATMENT**	**TOTAL**
INITIAL OUTCO-ME	**SUCCESS**	52	21	1	2	4	80
	DEFAULT	10	11	4	--	--	25
	FAILURE	2	3	--	--	--	5
	TOTAL	64	35	5	2	4	110

TABLE 6.2.10 UNIVARIATE ANALYSIS OF FACTORS CONTRIBUTING TO THE POOR OUTCOMES IN THE PATIENTS FOLLOWED UP

	POOR OUTCOME (N=46)	GOOD OUTCOME (N=64)	RELATIVE RISK	95% C.I	P-VALUE
MALE	42	51	1.92	0.79-4.65	0.09
MEALS<2/DAY	24	17	1.84	1.19-2.82	0.006*
SMOKING	30	27	1.74	1.08-2.81	0.017*
ALCOHOLIC	27	25	1.59	1.01-2.49	0.041*
DIABETES	7	5	1.47	0.086-2.51	0.21
EDUCATION </=5STD	32	31	1.71	1.03-2.82	0.027*
DEFAULT	15	10	1.65	1.07-2.52	0.036*
INTERUPTION OF RX	28	30	1.39	0.88-2.21	0.147
HIV INFECTION	5	1	2.17	1.41-3.34	0.029#
POOR HOUSING	31	20	2.39	1.47-3.90	0.0001*
FAMILY H/O TB	9	7	1.43	0.87-2.36	0.205

* = SIGNIFICANT

FISHER P=0.04 SIGNIFICANT

TABLE 6.2.11

MULTIVARIATE ANALYSIS OF RISK FACTORS FOR POOR OUTCOMES

	B	S.E.	Sig.	Exp(B)	95.0% C.I.for EXP(B)	
					Lower	Upper
HIV	**3.463**	**1.294**	**.007**	**31.918**	**2.529**	**402.815**
alcohol	**.700**	**.505**	**.166**	**2.014**	**.749**	**5.419**
meals	**1.064**	**.488**	**.029**	**2.899**	**1.114**	**7.546**
literacy	**.867**	**.537**	**.106**	**2.379**	**.831**	**6.812**
default	**.902**	**.538**	**.094**	**2.465**	**.858**	**7.082**
SMOKE	**.892**	**.516**	**.084**	**2.441**	**.888**	**6.709**
housing	**.864**	**.504**	**.086**	**2.373**	**.884**	**6.371**
Constant	**-2.916**	**.628**	**.000**	**.054**		

a Variable(s) entered on step 1: HIV, alcohol1, meals, lit, default, SMOKE, hou.

TABLE 6.2.12

DURATION OF FOLLOW UP- IN PERSON YEARS

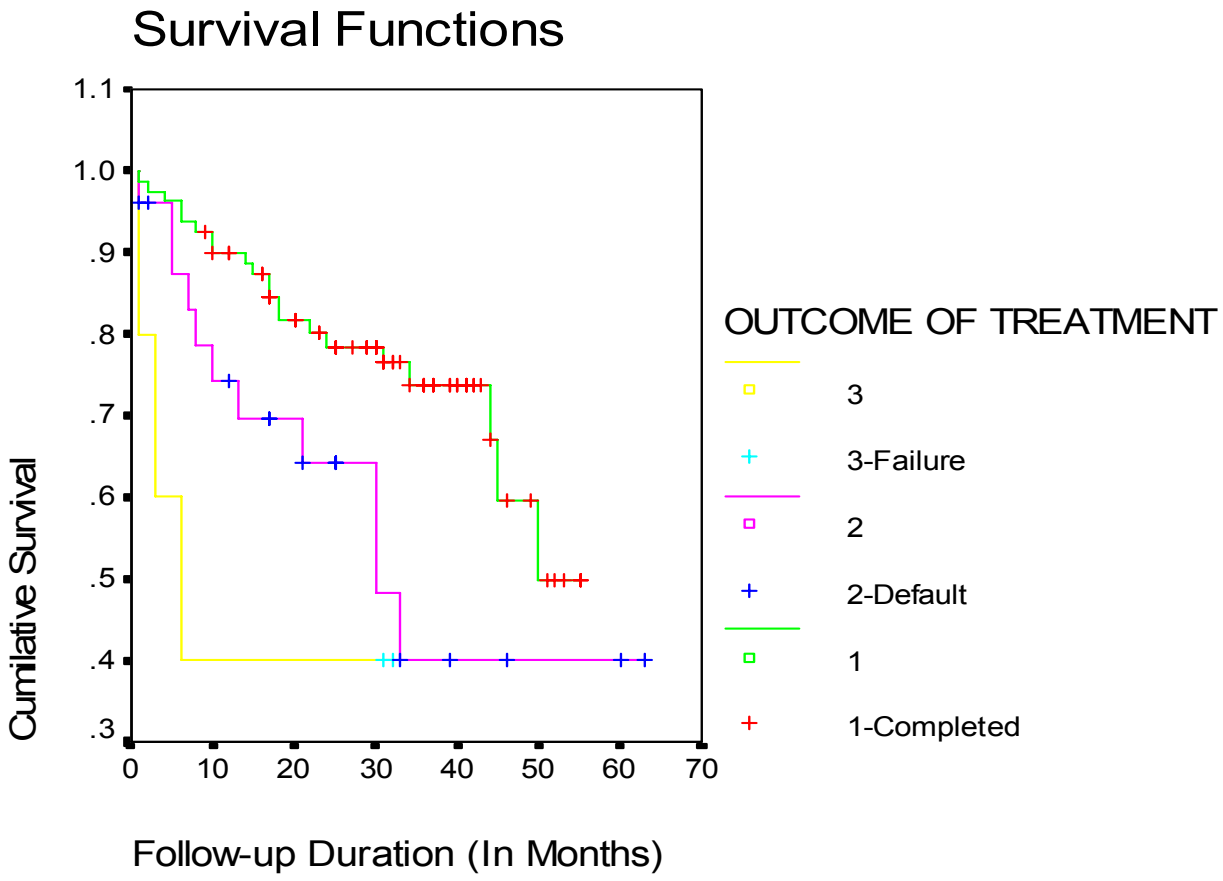
YEAR	PERSONYEARS	POOR OUTCOMES
2001	**52.25**	**10**
2002	**90.58**	**17**
2003	**70.25**	**11**
2004	**28**	**8**

TOTAL DURATION OF FOLLOW UP = 241 PERSON YEARS

CUMULATIVE DEATH RATE = 141.03 per 1000 persons years.

CUMULATIVE RELAPSE RATE = 24.88 per 1000 persons years follow up.

GRAPH 6.3 SURVIVAL ANALYSIS DEPENDING ON OUTCOME OF CAT II TREATMENT USING KAPLAN-MEIER SURVIVAL ANALYSIS FUNCTION



Statistic	df	Significance
Log Rank= 8.70	1	.0032

Table 6.2.13 CAUSE OF DEATH AMONG THOSE FOLLOWED UP.

CAUSE OF DEATH	Total
ALCOHOLIC LIVER DISEASE	1
CHRONIC RENAL FAILURE	1
CA-OESOPHAGUS	1
HIV/AIDS	3
MYOCARDIAL INFARCTION	2
PNEUMONIA	1
ACCIDENTAL	1
TB (NO OTHER ATTRIBUTABLE CAUSE)	26
Total	36

7. DISCUSSION

Many interventions have evolved for better control of tuberculosis over the last few decades.[45] Of these, many are aimed at making the treatment of tuberculosis simpler while maintaining effectiveness. The current WHO DOTS strategy brings as a package, all the essential elements required for effective tuberculosis control. Many National Tuberculosis Programs have adopted the DOTS strategy and showed consistently higher cure and completion rates.[46]

The analysis proceeds in two steps. First, study of patient profile and primary outcome and second on evaluation of current status.

Primary outcome refers to the outcome of at the end of treatment as defined by WHO DOTS strategy criteria. Current status has been divided into Sputum negative, Relapsed, Lost to follow up and Expired at follow up.

For evaluation of the primary outcome and patient profile, data from all 309 cases of patients who underwent CAT II antituberculosis treatment from CHAD/ CMC DOTS clinics between 2001 and 2004, analysed from the tuberculosis database and treatment cards.

This is then followed by analysis of the current status of the patients who were followed up by house visits from a defined geographical area comprised 110 patients out of 309 as per the sample size. Relapse rates and mortality are calculated using this data.

7.1 BASELINE CHARACTERISTCS (Refer Tables 6.1.1 & 6.1. 2)

Total number of 2345 patients had been started on DOTS from CHAD/CMC DOTS clinics from 2001 to 2004. Out of this category II treatment cases were 309 in total (13.2%).

Year wise break(table-6.1.1) up showed gradual decrease in percentage of Category II cases, which indirectly shows the efficiency of DOTS programme.

AGE AND SEX DISTRIBUTION OF PATIENTS ON CAT II ATT
(TABLE-6.1.3,6.1.4) AND GRAPHS (6.1.3.1,6.1.3.2)

Age distribution of patients showed the typical peaking in the productive age group (20 – 50 years) about 71.5% of the total cases.

Tuberculosis hinders the socioeconomic development of the country. 75% of people with tuberculosis are in the economically productive age group of 15–54 years as -quoted by different writers. Besides the disease burden, TB also causes an enormous socio-economic burden on India.[3]

Age and Sex distribution data showed more number of cases in females seen in lower age groups as compared to males. Not to forget less number of female patients .

Indication for Category II treatment showed 63.8% were due to relapse and 19.7% were due to default during earlier treatment. The duration between

completion of Cat I treatment to relapse ranged between 6 months to several years which triggered more interest in the investigation of relapse rates.

7.2 ANALYSIS OF PRIMARY OUTCOMES (Refer Tables 6.1. & 6.1.)

These outcomes are obtained from the data using the treatment cards of 309 Category II patients. Outcomes are categorized according to the WHO definitions[6]

Considering both cured and completed as treatment success -63.8%had successful outcome.

Cure rates in sputum positive patients was 61.94% is within the range of other studies where in Bangalore cohort had a cure rate of 39.8%.[8] vs Delhi study which had a better cure rates 73.3% .[39]

Default rate was 14.9% was less in comparison to other studies. Delhi study had a default rate of 16% against Bangalore cohort which had a high defaults of 43.8% where as overall default rate in India over 6 years as quoted by Dr. Fraser Wares – WHO India was 15.2%.[38]

Failure rate of 6.1% has to be followed further to rule out MDR TB.

Death rate was 13.3% during treatment might be due to severity of illness in people who come to Category II treatment.

Treatment success rates in patients who completed treatment as prescribed was 91.2% which is very encouraging.

Sputum status at initiation of treatment shows gradual decrease in highly infected cases over years.

Cross table on indication of treatment vs outcome shows better success rate among relapse patients compared to other indications.

Chances of Default patients going in to default again during treatment (23%) is statistically significant as compared to other indications.(RR1.78(1.01-3.12), Chi sq -3.9 and p=0.048)

Cat. II failure among patients with Cat. I failure was 24.2% which might indicate MDR TB. [47]

7.2 ANALYSIS OF THE CURRENT STATUS OF THE PATIENTS INTERVIEWED (Refer Section 6.2)

As per the sample size calculated 110 patients from a defined geographical area were followed up to their homes. (**APPENDIX I)**

7.2.2 OUTCOME OF THE INITIAL TREATMENT OF THE PATIENTS FOLLOWED UP (Refer Table 6.2.2)

Depending upon the primary outcome of treatment from the standard treatment cards , 80 people with treatment success , 25 default patients and 5 failure patients were visited from the accessible areas. Year-wise break up and indication for treatment has been given in table 6.2.1 and 6.2.2.

On follow up, it was found that majority of cases(71.2%) had been earlier treated with Cat I under RNTCP. Details regarding history of evolution of cat II could not be found in 30 cases esp in the death group. (TABLE 6.2.6)

Total duration of 241 person years were followed up.

Death, relapse and lost to follow up were considered as poor outcomes.

On follow up 58.1% were well. 31.8% had died during the period between completion of the treatment and follow up. Only two cases of relapse were found during the study. 4.5% of cases were lost to follow up due to migration or other causes. Four people (3.6%) who had already been retreated and cured were considered as relapsed.

Of the people with successful Cat.II treatment 62.1% had a good outcome on follow up as compared to 39% with defaults. There was no major statistical difference in follow up outcome between the sexes.

Cumulative death rate was 141.03 per 1000 persons years. Calculated by dividing total deaths by duration of follow up.

Relapse rates was 24.88 per 1000 persons years follow up. Only 2 sputums were found to be positive during follow up. Cases who had relapsed and retreated before follow up were also included in calculating relapse rates.

Survival analysis showed statistically significant difference among the different groups based on the Cat.II treatment outcomes. People who completed treatment as per the prescribed treatment have better survival compared to people who defaulted or treatment failures (Log Rank of 8.70 and significance of .0032).

RISK FACTORS FOR POOR OUTCOMES

Different attributes like diabetes, history of smoking, consumption of alcohol, HIV infection, male sex, housing, number of meals per day, history of default or interruption of treatment were considered as quoted by previous studies. In various reviews poor outcomes have been shown to have inconsistent relationship with demographic characteristics such as age, gender, marital status, alcoholism and others.[48]

Univariate analysis (Table 6.12) showed the significance relationship between HIV infection, education less than 5th standard, history of default, history

of smoking and alcohol consumption and meals less than two/day with poor outcomes.

Multivariate analysis showed only HIV co-infection and less than two meals per day as a significant risk factors for poor outcome when other risk factors were adjusted.(TABLE-6.13)

REASONS FOR INTERUPTION OF TREATMENT AS GIVEN BY PATIENTS

There were various reasons given by the patients for their defaulting on treatment. Severe illness and co-morbid conditions such as renal failure played an important in a few cases. Going out of station for work or due to monetary problems were other cited problems. Side effects of drugs and feeling better subjectively were other reasons. These are similar to the reasons given in other studies.[16, 17] About half of these defaults are probably preventable if the program can adapt itself to patient needs and problems. For example, education about the drugs side effects and transfer of patient-wise drug boxes to areas more accessible to the patient if he goes out of station for a while, can be some of the interventions.

Sub-study on patients knowledge regarding tuberculosis by questionnaire showed following factors.

1. Tuberculosis still considered as stigma,12(20%) respondents wanted to hide the factor that they had/were treated for T B, Reasons quoted were being unmarried, fear of loosing job among others.
2. Twenty two people did not know whether TB can be cured. Eight of them thought treatment of TB is life long.
3. 40 (66%) respondents said TB spreads through cough.
4. In 97% of patients their family people were supportive during illness.

7.7 SUMMARY

Tuberculosis remains a major public health problem in India.

There was a need to look at Cat II patients and their outcomes as very little literature was available on this topic.

This is a non-concurrent cohort study, which studied the category II patients(309) from standard TB treatment records maintained in the CHAD/CMC DOTS clinics from 2001 to 2004. A sample of this patients(110) from geographically accessible areas were followed up to know the current status and find relapse rates over time.

The data collected was analyzed using adequate statistical tests.

PATIENT PROFILE

Total number of 309 patients treated with category II ATT from 2001to 2004 were considered for the study.

- Cure rate of 61.94% among the sputum positive cases.
- Overall treatment success rate was 63.8%. However, successful outcome, among those completing the prescribed duration of treatment was 91.2% which is encouraging.
- Default rates of 14.9% are still high and needs to be tackled to improve outcome under programme conditions.

- Age distribution shows the typical pattern of TB affecting maximum the productive age groups. Cumulative incidence of 93.2% in age groups <60years.
- 13.3% of cases had died during treatment.

FOLLOW UP STUDY

Total number of 110 cases were followed up at their homes from a defined geographical area to find the current status and calculate relapse rates over time. Total period of follow up was 241 person years.

Average of 2.2 years of follow up per case.

1) Survival statistically better among treatment success patients as compared to defaults and failures.
2) Cumulative relapse rate was found to be 24.88 per 1000 persons years follow up.
3) Significant risk factors for poor out comes in the univariate analysis included educational status, housing, status of default, smoking habit, alcohol consumption, co-infection with HIV and inadequate food availability/intake. All these factors were statistically significant. Diabetes, family history of tuberculosis and male sex were found not to be significant.
4) Multivariate analysis showed HIVco-infection and inadequate food to be significant.

A cure rate of 61.94% and the success rate of 91.2% among Cases who took adequate treatment, supports the strength of Cat II as a standard re-treatment regimen. It suggests that regular the treatment under direct observation response is better. This gain is also visible on followup by better survival chances.

The study also underscores the importance of treatment adherence for achieving success.

8. LIMITATIONS OF THE STUDY

1) IN THE FOLLOW UP STUDY, the risk factors for poor outcomes especially deaths, were secured from the family members which may be biased.

2) True prevalence of HIV infection in this study population is not known as not everyone have been screened.

3) Adequate information could not be collected from few incomplete treatment cards .

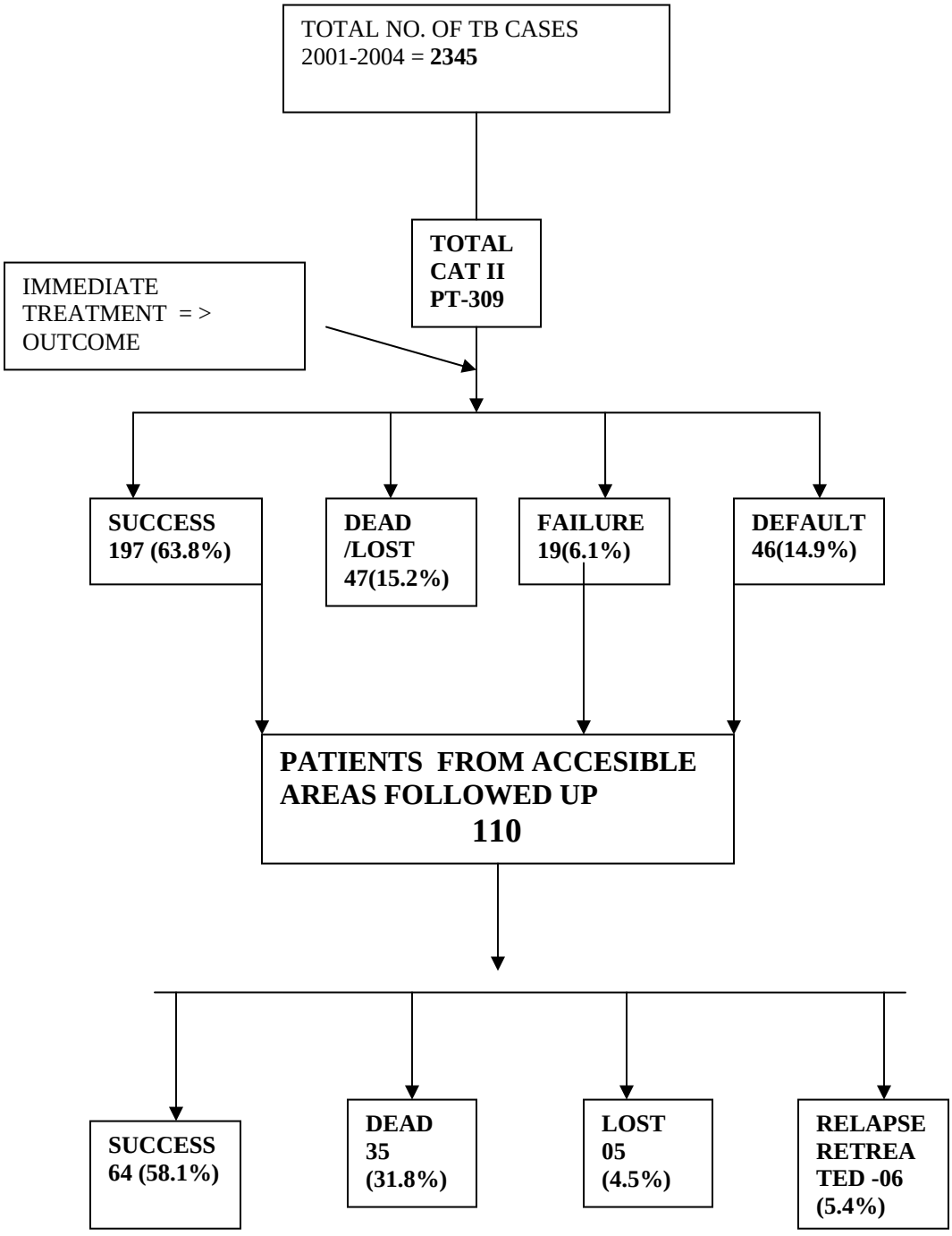
9. CONCLUSIONS

- Category II treatment under DOTS therapy still works with a success rate of 91.2% in patients who take prescribed duration of treatment as contrary to the belief that adding a single drug to a failing regimen will not help.

- Inadequate Food and HIV co-infection play a major role in poor outcomes

- Overall survival is better in treatment success patients.

APPENDIX I PATIENTS SELECTION AND FOLLOW UP FLOW CHART



APPENDIX II

LIST OF ABBREVIATIONS

AFB	Acid Fast Bacillus
ATT	Antituberculosis Treatment
BCG	Bacillus Calmette Guerrin
BMRC	British Medical Research Council
CDC	Centre for Disease Control
CHAD	Community Health and Development
CMC	Christian Medical college
CP	Continuation Phase
DANIDA	Danish International Development Agency
DFID	Danish Fund for International Development
DOT	Directly Observed Treatment
DOTS	Directly Observed Treatment - Short-course
DTC	District Tuberculosis Centre
IP	Intensive Phase
IUATLD	International Union Against Tuberculosis and Lung Disease
MO	Medical Officer
MOTC	Medical Officer Tuberculosis Control
NGO	Non-governmental Organisation
NTP	National Tuberculosis Program
PPM	Private-public mix
RNTCP	Revised National Tuberculosis Control Program
SAT	Self Administered Therapy
SCC	Short-course Chemotherapy
SIDA	Swedish International Development Agency
SPSS	Statistical Package for the Social Sciences
STLS	Senior Tuberculosis Laboratory Supervisor
STS	Senior Treatment Supervisor
TB	Tuberculosis
TRC	Tuerculosis Research Centre
TU	Tuberculosis Unit
WHO	World Health Organisation
PHC	Primary Health Centre

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